**Executive Summary**
**NIAID Reverse Genetics Workshop**
**Latham Hotel-Georgetown, Washington D.C.**
**July 9-10, 2001**

In response to three recent developments in influenza biology and molecular biology, the Influenza Virus Program, Respiratory Diseases Branch, Division of Microbiology and Infectious Diseases (DMID), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) organized a workshop on influenza virus reverse genetics. The three recent developments related to: (1) the development of reverse genetics methodologies to the point where it is now possible to rapidly and readily generate infectious influenza virus containing any combination of RNA segments derived from the range of human and animal influenza strains; (2) the recognition in Hong Kong of transmission of avian strains of virus to human and the occurrence of illness and death in a very small proportion of individuals infected with these viruses; and (3) the use of molecular biological techniques to rescue and initiate sequencing of the 1918 pandemic influenza virus from fixed pathologic tissue and a permafrost-preserved cadaver.

The NIAID recognized that these developments provided potential for new insights into influenza biology that could facilitate vaccine and antiviral development as well as could serve as a cause of public concern. The workshop brought together an international group of researchers in influenza viruses; and scientists outside of the influenza field with research experience in other human viruses, in biosafety and in public policy.

The participants were asked to discuss several broad issues relating to biosafety of the natural and recombinant viruses and, specifically to the potential to generate 1918 like strains and recombinants. Several brief overviews and status reports were made on these areas. Presentations were also made by representatives of the U.S. Department of Agriculture (USDA), the Centers for Disease Control and Prevention (CDC), the NIH Occupational Health and Safety Branch and the NIH Office of Biotechnology Activities (OBA). References were made to the Center for Disease Control Document, Biosafety in Microbiological and Biomedical Laboratories (BM/BL)[1] and to the NIH Guidelines for Recombinant DNA and Gene Transfer.[2]

In designing safety approaches and procedures, there are a number of issues to consider including the properties and nature of the agent, how the agent will be studied, and availability of vaccines and treatments for the organisms. Progressively more stringent procedures are put into place depending on these factors. Plans and procedures for documenting and reacting to laboratory accidents/incidents need to be in place. An example of developing and implementing such strategies was the CDC approach to devising specific plans and procedures for protecting laboratory personnel who would be working with the avian influenza isolates from Hong Kong, such as H5N1, which were infectious for humans.

---

[1] Biosafety in Microbiological and Biomedical Laboratories, 4th Edition, May 1999. <http://bmbl.od.nih.gov/index.htm>

[2] http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html

The NIH Guidelines for Recombinant DNA and Gene Therapy classify influenza as Risk-Group 2, and require Institutional Biosafety Committee (IBC) approval for recombinant DNA research. The IBC considers, on a case-by-case basis, the characteristics of the agent and how it will be used. The IBC can obtain Ad Hoc expertise, contact the NIH Office of Biotechnology Activities[3] for assistance or request the Recombinant DNA Advisory Committee advice. The representative from the NIH Occupational Health and Safety Branch briefly summarized the working group process that was used to develop the HIV guidelines, which also use the approach of risk assessment for the specific proposed studies.

The participants noted that the vast majority of influenza viruses can be safely studied under the current BL-2 procedures, but that there exceptions of zoonotic agents, such as H5 and H7, that may needed to be assessed for higher levels of biosafety. There have not been laboratory outbreaks of influenza reported over the long number of years that influenza viruses and recombinants have been studied in laboratory and animal experiments. While the new technologies using plasmids to construct recombinant influenza viruses and make specific mutants are quicker, easier and more precise, influenza recombinants and mutants have been made in the laboratory for a number of years using more laborious methods. Understanding the basis for the high mortality and the unusual mortality pattern in the 1918 virus could provide important knowledge for understanding influenza pathogenesis and for developing prevention strategies.

With respect to biosafety procedures, it is not possible to anticipate the totality of experiments in an area of rapidly evolving science or to consider the variety of individual facilities that exist in U.S. academic and government laboratories. Thus, rather than trying to develop specific guidelines for the numerous and varied kinds of potential experiments and recombinants viruses, it was most appropriate to have local biosafety committees examine the specific planned work and make risk assessments and safety recommendations. As a guide to such IBC groups who frequently use the BM/BL as a reference resource, it was proposed that a working group be organized to provide updated language for the BM/BL Influenza Subsection entitled, "Activities Utilizing Noncontemporary Virus Strains." The draft language would be circulated for comment and discussion.

At the current pace of progress, it will take three to five years before a full 1918-like virus could be close to being assembled. It was therefore proposed that another consensus meeting on the 1918 virus be held at a future time when more data would be available.

Influenza research has been and will remain a major interest of the NIAID. With respect to the use of reverse genetics and studies of strains derived by this technology, the workshop participants noted that while caution is needed until there was more information about the biological properties of avian viruses, new recombinant viruses, and 1918-like viruses, there is potential for studies of these viruses to produce knowledge about the pathogenicity of influenza viruses and to aid in the development of vaccines, antiviral and surveillance strategies.

[3] E-mail: oba@od.nih.gov

| | |
|---|---|
| Filename: | reverse.doc |
| Directory: | X:\influenza |
| Template: | Normal.dot |
| Title: | Meeting Summary |
| Subject: | |
| Author: | susan spring |
| Keywords: | |
| Comments: | |
| Creation Date: | 11/12/2004 2:03:00 PM |
| Change Number: | 2 |
| Last Saved On: | 11/12/2004 2:03:00 PM |
| Last Saved By: | Ibm Customer |
| Total Editing Time: | 5 Minutes |
| Last Printed On: | 5/3/2005 10:25:00 AM |

As of Last Complete Printing

| | |
|---|---|
| Number of Pages: | 2 |
| Number of Words: | 946 (approx.) |
| Number of Characters: | 5,397 (approx.) |